# SUMMARY OF SAFETY AND EFFECTIVENESS DATA

## I. GENERAL INFORMATION

| | |
|---|---|
| DEVICE GENERIC NAME: | Intervertebral Cervical Cage |
| DEVICE TRADE NAME: | AFFINITY™ Anterior Cervical Cage System |
| APPLICANT'S NAME: | Medtronic Sofamor Danek USA<br>1800 Pyramid Place<br>Memphis, TN 38132 |
| DATE OF PANEL RECOMMENDATION: | None |
| PREMARKET APPROVAL (PMA) APPLICATION NUMBER: | P000028 |
| DATE OF NOTICE OF APPROVAL TO THE APPLICANT: | June 13, 2002 |

## II. INDICATIONS FOR USE

The AFFINITY™ Anterior Cervical Cage System (hereinafter called the AFFINITY™ Cage) is indicated for anterior cervical interbody fusion procedures in skeletally mature patients with cervical disc disease at one level from the C2-C3 disc to the C7-T1 disc. Cervical disc disease is defined as intractable radiculopathy and/or myelopathy with herniated disc and/or osteophyte formation on posterior vertebral endplates producing symptomatic nerve root and/or spinal cord compression confirmed by radiographic studies. AFFINITY™ implants are to be used with autogenous bone graft and implanted via an open, anterior approach.

## III. CONTRAINDICATIONS

The AFFINITY™ Anterior Cervical Cage System should not be implanted in patients with an active infection or with an allergy to titanium or titanium alloy.

## IV. PRECAUTIONS

The AFFINITY™ Cage System should only be used by surgeons who are experienced in cervical interbody fusion procedures and have undergone adequate training with this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, such as neurological complications.

## V. DEVICE DESCRIPTION

The Affinity™ Cage System consists of hollow, threaded, tapered metal devices implanted into the intervertebral disc space. The implants employ the following design characteristics:

- Implants are manufactured from titanium alloy (Ti-6Al-4V, ASTM F136).
- Implants have a continuous screw thread on the outer surface for purchase into the vertebral endplates. The implants are tapered (8° taper).
- There are circular and elongated transverse holes along the length of the implant to allow for bony ingrowth. During implantation, the cage is rotated so that the two elongated holes on opposite sides of the implant are aligned with the vertebral endplates.
- The anterior end is the wider end and is open to receive autologous bone graft and to mate with the implantation instrument. The posterior end of the implant is closed.
- Autologous bone is taken from the iliac crest and packed into the open (anterior) end of the cage prior to insertion.
- The device is available in the following 14 sizes (minor diameter x length):

**Table I – Implant Sizes**

| Implant Sizes (minor diameter x length) | | Number of Implants per Spinal Level | |
|---|---|---|---|
| | | One | Two |
| 6 x 12mm | 6 x 14mm | | x |
| 7 x 12mm | 7 x 14mm | x | x |
| 8 x 12mm | 8 x 14mm | x | x |
| 9 x 12mm | 9 x 14mm | x | |
| 10 x 12mm | 10 x 14mm | x | |
| 11 x 12mm | 11 x 14mm | x | |
| 12 x 12mm | 12 x 14mm | x | |

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative surgical treatments include, but are not limited to, various bone grafting techniques (e.g., Cloward bone dowels, Smith Robinson tri-cortical wedges, and Keystone grafts) sometimes used in conjunction with anterior/anterolateral spinal systems (e.g., plate and screw systems), or posterior spinal systems (e.g., screw/rod, plate systems, posterior wiring systems). In addition, treatment with the BAK/Cervical Interbody Fusion System is an alternative surgical treatment. Non-fusion surgical techniques, such as posterior decompression may also be utilized.

Nonoperative alternative treatments include, but are not limited to, physical therapy, medication, braces, chiropractic care, bed rest, traction, heat, spinal injections, or exercise programs.

## VII. MARKETING HISTORY

The AFFINITY™ Cage has a marketing history outside the United States, including Europe, Australia, Japan, and Canada. The AFFINITY™ Cage has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

## VIII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

An investigational device exemptions (IDE) study of the AFFINITY™ Cage System was performed (G960201). A total of 202 AFFINITY™ device patients and 62 control (single level anterior interbody fusion procedure using autogenous bone graft from the iliac crest) patients were enrolled in a multi-center clinical study. In the AFFINITY™ patient group, the most common adverse events were neck and/or arm pain, trauma, subsequent spinal event, gastrointestinal complication, and neurological event. See Table II for a summary of adverse event rates observed in the clinical study; events are listed in alphabetical order. Table III presents the Bayesian statistical comparison of adverse events between the AFFINITY™ device group and the control treatment group. Table IV summarizes the secondary surgical interventions in the AFFINITY™ device and control treatment groups in the 12-Month and 24-Month post-operative intervals. Table IV also presents the Bayesian statistical comparison of secondary surgeries between the AFFINITY™ device group and the control treatment group.

## TABLE II - ADVERSE EVENTS

| Adverse Event | Surgery | | Postoperative (1 day to 1 Month) | | 6 Weeks (1 Month to 2 Months) | | 3 Months (2 Months to 5 Months) | | 6 Months (5 Months to 9 Months) | | 12 Months (9 Months to 19 Months) | | 24 Months (or greater) (19 Months to 48 Months) | | Total Adverse Events | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AFFINITY N=202 | Control[1] N=62 | AFFINITY N=202 | Control N=62 | AFFINITY N=200 | Control N=58 | AFFINITY N=191 | Control N=58 | AFFINITY N=186 | Control N=57 | AFFINITY N=178 | Control N=50 | AFFINITY N=174 | Control N=47 | AFFINITY | Control |
| Anatomical/ Technical Difficulty | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 |
| Cancer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 2 | 0 |
| Cardio/Vascular | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 1 | 5 | 6 |
| Carpal Tunnel Syndrome | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 5 | 0 | 0 | 0 | 7 | 0 |
| Dural Tear | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Dysphonia/Dysphagia | 0 | 0 | 5 | 4 | 3 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 6 |
| Gastrointestinal | 0 | 0 | 7 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 5 | 1 | 3 | 0 | 16 | 2 |
| Graft Site Related | 0 | 0 | 5 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 3 |
| Implant Displacement/ Loosening Collapse | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 0 | 2 | 0 | 1 | 0 | 0 | 0 | 9 |
| Infection | 0 | 0 | 5 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 2 | 7 | 5 |
| Malpositioned Implant | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Neck and/or Arm Pain | 0 | 0 | 2 | 0 | 7 | 0 | 5 | 2 | 5 | 1 | 10 | 2 | 6 | 1 | 35 | 6 |
| Neurological | | | | | | | | | | | | | | | | |
| Upper Body[2] | 0 | 0 | 1 | 4 | 3 | 1 | 1 | 3 | 0 | 3 | 5 | 2 | 3 | 4 | 13 | 17 |
| Lower Body[3] | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | 1 | 0 | 2 | 5 |
| Non-Union[4] | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 3 | 2 | 2 | 1 | 3 | 2 | 8 | 5 |
| Non-Union Pending[5] | 0 | 0 | 0 | 0 | 0 | 0 | | 3 | 1 | 0 | 1 | 2 | 1 | 0 | 4 | 5 |
| Other Pain[6] | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 2 | 0 | 5 | 1 | 3 | 2 | 13 | 4 |
| Respiratory | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| Spinal Event: | | | | | | | | | | | | | | | | |
| Cervical Spine | 0 | 0 | 0 | 0 | 2 | 0 | 3 | 3 | 2 | 0 | 5 | 3 | 3 | 2 | 15 | 8 |
| Thoracic Spine | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Lumbar Spine | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 5 | 1 | 2 | 0 | 1 | 0 | 13 | 1 |
| Subsidence | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Trauma | 0 | 0 | 3 | 0 | 1 | 0 | 10 | 1 | 6 | 1 | 5 | 0 | 5 | 4 | 30 | 6 |
| Urogenital | 0 | 0 | 2 | 4 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 5 | 5 |
| Vascular Intra-op | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Other[7] | 0 | 0 | 3 | 2 | 1 | 0 | 0 | 1 | 0 | 1 | 6 | 1 | 6 | 4 | 16 | 9 |

[1] Control = Single level anterior interbody fusion procedure using autogenous bone graft from the iliac crest.
[2] Neurological adverse events that affected the upper body, i.e., arms, neck, etc.
[3] Neurological adverse events that affected the lower body, i.e, legs, feet, etc.
[4] Non-union adverse events that have resulted in a second surgery.
[5] Non-union adverse events that have not resulted in a second surgery.
[6] "Other pain" consists of pain that is not related to the surgery or the treatment area. Examples are bursitis, knee pain, back pain, migraine headaches.
[7] The "Other" adverse event category consists of the following adverse events reported in the clinical trial: allergy/rash, allergic reaction to chemotherapy, chemotherapy side effects, cholecystectomy, diabetes, elevated temperature, fibromyalgia, hardware removal, hearing loss and cataracts, hepatomegaly, Horner's Syndrome, joint crepitus, low B12 and folate, malpositioned cervical plate, narcotic addiction, psychological disorder, and toothache.

The most noteworthy adverse events in the AFFINITY™ device group were neurological complications and spinal events. A total of 15 upper and lower body neurological events occurred in 15 patients in the AFFINITY™ device group. These events included: 9 events of tingling and/or numbness in arms or hands either with or without associated pain; 2 cases of new myelopathy; 1 event producing leg numbness symptoms; 1 case of hand cramping; 1 Morton's neuroma of the foot; and 1 median nerve entrapment which was not carpal tunnel.

A total of 29 spinal events occurred in 27 patients in the AFFINITY™ device group. These events included the following: 6 cervical spondyloses, 4 cases of herniated nucleus pulposus in the cervical spine; 3 cervical degenerative disc disease; 1 cervical arthritis; 1 bone spur; 1 thoracic herniated nucleus pulposus and 13 lumbar associated events, such as degenerative disc disease.

In addition, there were 29 patients in the AFFINITY™ device group who had 35 reports of neck and/or arm pain. Of the 14 events reported between surgery discharge and 6 months postoperatively, 7 involved neck pain including muscle cramps or strains, 6 involved shoulder or arm pain including rotator cuff injuries, and 1 involved hand pain. Of the 10 events occurring between 6 and 12 months postoperatively, 5 involved neck and arm pain, 4 involved shoulder pain including 1 rotator cuff tendonitis, and 1 involved cervical muscle pain and headache. Eleven events occurred at least 12 months after the initial surgery. Of these, 3 involved shoulder pain, 4 involved neck and/or arm pain, 1 involved arm pain associated with fatigue, 1 involved joint pain in neck, shoulders, back, and hands, 1 involved elbow pain, and 1 involved thoracic pain.

In addition to the 35 reports of neck/arm pain, Table II includes 15 patients who reported hand pain. Of the 50 patients reporting neck/arm/hand pain symptoms, 35 of the complaints could be attributed to the operative or adjacent levels. Of the 50 patients complaining of postoperative neck, arm and hand symptoms, 10 were considered neck pain failures and 7 were considered arm pain failures according to the success/failure criteria.

Table III presents the Bayesian statistical comparison of adverse events between the AFFINITY™ device group and the control treatment group.

| Table III - Bayesian Comparison of Adverse Events | | |
|---|---|---|
| **Adverse Event** | **There is a 95% Probability that adverse event rates will fall between the following ranges** | |
| | **AFFINITY ™ Device** | **Control** |
| Anatomical/Technical Difficulty | 0% to 3% | 2% to 13% |
| Cancer | 0% to 4% | 0% to 6% |
| Cardio/Vascular | 2% to 32% | 6% to 52% |
| Carpal Tunnel | 2% to 7% | 0% to 6% |
| Dural Tear | 0% to 3% | 0% to 6% |
| Dysphonia/Dysphagia | 3% to 11% | 2% to 15% |
| Gastrointestinal | 6% to 15% | 1% to 9% |
| Graft Site Related | 2% to 47% | 3% to 54% |
| Implant Collapse/ Displacement/Loosening | 0% to 2% | 8% to 25% |
| Infection | 2% to 10% | 0% to 12% |
| Malpositioned Implant | 0% to 3% | 0% to 6% |
| Neck and/or Arm Pain | 12% to 23% | 3% to 16% |
| Neurological | 4% to 12% | 26% to 53% |
| Non-Union (Outcome Pending) | 1% to 7% | 2% to 21% |
| Other Pain | 3% to 11% | 2% to 19% |
| Respiratory | 0% to 2% | 1% to 11% |
| Spinal Event | 10% to 23% | 7% to 27% |
| Subsidence | 0% to 3% | 0% to 6% |
| Trauma | 5% to 47% | 6% to 35% |
| Urogenital | 1% to 7% | 3% to 23% |
| Vascular Intraop | 0% to 2% | 0% to 9% |
| Other Adverse Event | 5% to 13% | 5% to 24% |
| Any Adverse Event | 46% to 60% | 55% to 81% |

Some of the adverse events led to surgical interventions subsequent to the clinical trial surgery. These surgical interventions can be classified as revisions, removals, supplemental fixations, reoperations, and other (see footnotes below Table IV for an explanation of these terms). Table IV summarizes the secondary surgical interventions in the AFFINITY™ device and control treatment groups in the 12-Month and 24-Month post-operative intervals. Table IV also presents the Bayesian statistical comparison of secondary surgeries between the AFFINITY™ device group and the control treatment group.

| Table IV - Secondary Surgical Procedures | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Clinical Comparison of Secondary Surgeries | | | | | | | Bayesian Statistical Comparison of Second Surgeries | |
| Type of Secondary Surgical Procedure | Up to 12 Months (1 day to 19 Months) | | 24 Months or Later (19 Months to 48 Months) | | Total Events[4] | | There is a 95% Probability that Second Surgery rates will fall between the following ranges | |
| Type of Secondary Surgical Procedure[3] | AFFINITY™ N=178 | Control[1] N=50 | AFFINITY™ N=174 | Control N=47 | AFFINITY™ | Control | AFFINITY™ Cage System | Control |
| Revision | 3 | 5 | 0 | 2 | 3 | 7 | 1% to 31% | 6% to 58% |
| Removal | 2 | 0 | 3 | 0 | 5 | 0 | 1% to 6% | 0% to 6% |
| Supplemental Fixation | 5 | 0 | 1 | 0 | 6 | 0 | 1% to 6% | 0% to 6% |
| Reoperation | 1 | 2 | 1 | 0 | 2 | 2 | 0% to 4% | 1% to 11% |
| Other[2] | 27 | 5 | 4 | 3 | 31 | 8 | 9% to 19% | 8% to 30% |

[1] Control = Single level anterior interbody fusion procedure using autogenous bone graft from the iliac crest.
[2] Other Second Surgery is any surgical procedure not classified as a revision, removal, supplemental fixation, or a reoperation such as surgeries for hernias, rotator cuff tears, lumbar adverse events, carpal tunnel syndrome, cervical adverse events that occurred at a different level, etc.
[3] **Revision:** A procedure that adjusts or in any way modifies the original implant configuration.
**Removal:** A procedure at the involved level that removes one or more components of the original implant configuration without replacement with the same type of trial device.
**Supplemental Fixation:** A procedure at the involved level in which additional cervical fixation devices that are not approved as part of the protocol are placed.
**Reoperation:** Any surgical procedure at the involved level that is not classified as a Removal, Revision, or Supplemental Fixation, such as a procedure for wound drainage of the graft site.
**Other:** Any surgical procedure not classified as a revision, removal, supplemental fixation, or a reoperation, such as surgeries for hernias, rotator cuff tears, lumbar adverse events, carpal tunnel syndrome, cervical adverse events that occurred at a different level, etc.
[4] Some patients experienced more than one second surgery.

Of the 47 patients in the AFFINITY™ device group who required a second surgery, 8 had surgery for non-union, 7 had surgery for neck and/or arm pain, 5 had surgery to treat a lumbar condition, 5 required surgery due to trauma, and 3 had surgery to treat carpal tunnel syndrome. Most of the second surgeries occurred up to and including the 12-Month post-operative interval.

## IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The following is a list of potential adverse events which may occur with cervical interbody fusion surgery with the AFFINITY™ Cage System. Some of these adverse events have been previously reported in the adverse events table.

- Bending, breakage, loosening, and/or migration of components
- Foreign body (allergic) reaction

- Tissue or nerve damage
- Post-operative change in spinal curvature, loss of correction, height, and/or reduction
- Infection
- Dural tears
- Neurological system compromise
- Dysphagia/dysphonia
- Scar formation
- Bone fracture
- Non-union (or pseudarthrosis), delayed union, mal-union
- Cessation of any potential growth of the operated portion of the spine. Loss of spinal mobility or function
- Graft donor site complications
- Damage to blood vessels and cardiovascular system compromise
- Gastrointestinal complications
- Damage to internal organs and connective tissue
- Development of respiratory problems
- Incisional complications
- Change in mental status
- Death

**Note:** Additional surgery may be necessary to correct some of these potential adverse events.

## X. SUMMARY OF PRECLINICAL STUDIES

**Laboratory Studies**

Table V summarizes the laboratory studies performed on the AFFINITY™ Cage. A Finite Element Analysis (FEA) was conducted and confirms that, of the

7-12mm diameter implants, the 7mm device is the worst case. Note: The surgical protocol limits implantation of the 6mm implant to 2 per level.

**Table V – Laboratory Studies**

| Study | Results/Conclusions |
|---|---|
| **Static Axial Compressive Yield Load**, 7mm implant (n=5)<br>Samples were loaded at 60mm/min and the ultimate compressive loads were measured. | **34,660 ± 699 N**<br>Therefore, the device should withstand anticipated loads in the cervical spine.<br>NOTE: Medtronic Sofamor Danek estimated the compressive strength of cervical bone graft constructs based on strengths published in the literature. White's[1] research reports the strength of cervical bone constructs as ranging from 2,312 to 3,028 N; Wittenberg's[2] research determined the strength to range from 789 to 5,070 N. |
| **Compressive Fatigue Strength**, 7mm implant (n=10)<br>Samples were tested at 10Hz until failure or run-out to 5 million cycles. | **Implant survived 5 million cycles at 1,730 N.**<br>Therefore, the device should withstand anticipated loads in the cervical spine.<br>NOTE: According to White and Panjabi[3], the maximum compressive load in the cervical intervertebral disc is 74 N. |
| **Insertion Torque**, 9 x 14mm implant (n=3)<br>Human cadaver spines were potted from C2-T1 in PMMA and implants were placed at the C4-C5 level. The implant size tested was based on the size which best fit the disc height and vertebral body depth. | **1.15 ± 0.63 Nm**<br>This result compares favorably with the insertion torques of 3 lumbar cages:<br>• NOVUS LT: 0.95 Nm<br>• NOVUS LC: 0.87 Nm<br>• Spine-Tech BAK: 0.74 Nm |
| **Push-Out Strength**, 7 x 12mm implant (n=5)<br>Testing was conducted in accordance with ASTM Draft Standard F04.25.02.02. Each cage was placed between two foam blocks with a 100N pre-load. | **347 ± 42 N**<br>This is higher than the push-out strength measured for a 14 x 20mm bone dowel (i.e., 199 ± 50 N) when tested in the same manner. |

## XI. SUMMARY OF CLINICAL STUDIES

### A. Objectives

The objective of the clinical study was to assess the safety and effectiveness of the AFFINITY™ Anterior Cervical Cage System in the treatment of cervical disc disease.

### B. Study Design

The clinical study for the AFFINITY™ Anterior Cervical Cage System compared AFFINITY™ implants to a single-level anterior interbody fusion procedure using autogenous bone graft from the iliac crest. The multi-center, prospective, non-randomized, controlled investigation was designed as an equivalence trial. Treatment patients were enrolled at separate sites than control patients. The effectiveness measures selected for this investigation evaluated whether the implanted disc level was fused, whether there was an improvement in neck pain and disability, whether neurological status was maintained or improved, and whether there were improvements in a patient's general health. Safety information was measured by an analysis of reported adverse events and second surgeries .

## C. Inclusion and Exclusion Criteria

Patients were enrolled in this study according to the following inclusion/exclusion criteria:

*Inclusion criteria*

- Symptomatic cervical disc disease, as defined by intractable radiculopathy and/or myelopathy with herniated disc and/or osteophyte formation on posterior vertebral endplates producing symptomatic nerve root and/or spinal cord compression which is documented by diagnostic imaging findings
- Single level involvement from C2-C3 disc to C7-T1 disc
- Unresponsive to 6 weeks conservative, nonoperative treatment, or has the presence of progressive symptoms or signs of nerve root or spinal cord compression in face on continued nonoperative management
- Age ≥18 years

*Exclusion criteria*

- Previous surgical intervention at the involved level
- Severe osteopenia, osteoporosis, osteomalacia, or metabolic bone disease
- Overt or active spinal and/or systemic infection
- Instability greater than 3.5mm translation, or 11° of angular motion
- Condition that required postoperative medications that interfere with fusion, such as steroids
- Known metal allergy
- Mental incompetence
- Prisoner status
- Pregnancy
- Alcohol or drug abuse

## D. Patient Assessments

Patient follow-up examinations were performed preoperatively, perioperatively and postoperatively at 6 weeks, 3 months, 6 months, 12 months, 24 months, and biennially after the 24-month time point. The effectiveness variables included assessment of fusion, pain/disability status according to the Neck Disability Index (NDI), neck pain, arm pain, neurological status, general health status, disc height status, and overall success.

*Outcomes Assessed and Success Criteria:*

- Fusion was assessed by independent review of lateral flexion/extension (F/E) and anterior/posterior (A/P) radiographs. Fusion success was

defined as ≤4° of motion on lateral F/E radiographs and no evidence of radiolucency >2mm covering more than half of either the superior or inferior surface of the implant or graft. Also, patients having secondary surgeries due to nonunions were considered fusion failures.

- Pain/disability status were assessed using the Neck Disability Index (NDI). Pain/disability success was based on the postoperative NDI score being better than the preoperative score by at least 15 points if the preoperative score were at least 30 points or by at least 50% if the preoperative score were less than 30 points. If the preoperative NDI score were zero, the postoperative score also had to be zero for success.

- Neck pain was rated on a 5-point scale. Neck pain success was defined as maintenance or improvement in the score.

- Arm pain was rated on a 5-point scale. Arm pain success was defined as maintenance or improvement in the score.

- Neurologic status included an assessment of motor function, sensory, reflexes, and the foraminal compression reproducing pain. Neurological status success was defined as maintenance or improvement in the status.

- General health was assessed with the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). General health success was defined as maintenance or improvement in the SF-36 subscores, the physical component score (PCS), and mental component score (MCS).

- Disc height measurements were taken from radiographs. Disc height success was defined as no more than a 2mm decrease in the anterior or posterior post-operative disc heights relative to the pre-operative measurements.

- Overall success was defined as a patient demonstrating fusion, a successful pain and disability outcome, neurological success as well as the patient not having a secondary surgery classified as a revision, removal or supplemental fixation.

## E. Demographic Data

A total of 202 patients were entered in the AFFINITY™ device clinical trial. A total of 62 control patients were also entered into the clinical trial from two U.S. studies and two U.K. studies.

Demographic information pertaining to the patients participating in these clinical trials is presented in Table VI.

| TABLE VI – DEMOGRAPHIC INFORMATION | | |
|---|---|---|
| | **AFFINITY™ Device** N=202 | **Control** N=62 |
| Age (yr.) Mean [Range] | 44.5 [27-76] | 50.1 [27-85] |
| Weight (lbs.) Mean [Range] | 178.6 [97-280] | 172.1 [115-270] |
| Height (in.) Mean [Range] | 67.5 [59-76] | 67.1 [60-73.5] |
| Sex - Freq. (%) | | |
| Male | 105 (52.0%) | 35 (56.5%) |
| Female | 97 (48.0%) | 27 (43.5%) |
| Tobacco used - Freq. (%) | | |
| Yes | 73 (36.1%) | 30 (48.4%) |
| No | 129 (63.9%) | 32 (51.6%) |
| Workers Comp. - Freq. (%) | | |
| Yes | 44 (21.8%) | 4 (6.5%) |
| No | 158 (78.2%) | 58 (93.5%) |
| Taking Preop. Medication for Pain - Freq. (%) | | |
| Yes | 148 (73.3%) | 38 (61.3%) |
| No | 54 (26.7%) | 24 (38.7%) |
| Previous Back Surgery – Freq. (%) | | |
| Yes | 14 (6.9%) | 1 (1.6%) |
| No | 188 (93.1%) | 61 (98.4%) |

Comparisons between the AFFINITY™ treatment group and the control group demographics demonstrated some differences that potentially favored the AFFINITY™ patients. Medtronic Sofamor Danek addressed these potential differences in their statistical analyses. All preoperative variables were considered as covariate candidates and the five most important ones, gender, preoperative work status, tobacco use, neurological compression test (F.C.T.) reaction, and whether a patient had preoperative radicular symptoms, were incorporated into covariate analyses of the outcome parameters, thereby adjusting the posterior probabilities in accordance with their influence. Consequently, based on this statistical methodology, most important prognostic differences between the two treatment groups for demographic and preoperative information have been taken into account in assessing the outcome parameters.

## F. Patient Accountability

The database was closed for analysis as of April 5, 2001. The patient accountability data are summarized in Table VII.

| Table VII –Patient Accountability | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Treatment Group** | **Preoperative** x/n (%) | **Surgery/ Discharge** x/n (%) | **6 Weeks** x/n (%) | **3 Months** x/n (%) | **6 Months** x/n (%) | **12 Months** x/n (%) | **24 Months** x/n (%) |
| AFFINITY™ Device | 202/202 (100) | 202/202 (100) | 200/202 (99.0) | 191/202 (94.6) | 186/201 (92.5) | 178/197 (90.4) | 174/192 (90.6) |
| Control | 62/62 (100) | 62/62 (100) | 58/59 (98.3) | 58/59 (98.3) | 57/59 (96.6) | 50/55 (90.9) | 47/50 (94) |

## G. Data Analyses and Results

The results of the clinical study were evaluated using Bayesian statistical methods. All patients involved in the clinical trial of the AFFINITY™ Anterior Cervical Cage System and the control group studies were enrolled under the same inclusion/exclusion criteria. To substantiate the comparability of the two groups, a logistic regression analysis was performed which examined the relationship of all demographic, preoperative medical conditions and preoperative measurements of effectiveness variables on the overall success results. All preoperative variables were considered as covariate candidates and the five most influential ones (gender, preoperative work status, tobacco use, neurological compression test (F.C.T.) reaction, and whether a patient had preoperative radicular symptoms) were incorporated into covariate analyses of the outcome parameters, thereby adjusting the posterior probabilities in accordance with their influence. Consequently, based on this statistical methodology, the most influential prognostic differences between the two treatment groups for demographic and preoperative information were taken into account in assessing the outcome parameters.

A small fraction of the patients did not have their 24-month postoperative evaluations when the results were analyzed. Their 24-month results were predicted from their 12-month outcomes and the relationship established from patients that had both 12 and 24-month evaluations.

### 1. Effectiveness Analysis

As previously stated, the effectiveness analysis included assessment of fusion at the involved level, pain/disability status, neck pain, arm pain, neurological status, general health status, disc height status, and overall success. In some cases, only partial data were available (i.e., not all of the outcome measures were obtained for all patients at all follow-up points). In these cases, all available outcomes were summarized in the analyses. Therefore, the number of patients included in the assessment of the outcomes varies slightly due to missing data. The effectiveness analyses involved the comparison of the AFFINITY™ device group to the control group.

The adjusted posterior means of success probabilities for the primary effectiveness parameters, including overall success, at 24 months postoperative can be found in Table VIII.

**Table VIII – Posterior Means (95% HPD Credible Intervals) of Success Probabilities for Primary Effectiveness Variables**

| | 24 Months | |
|---|---|---|
| | **AFFINITY™ Device** Success Rate (Range[1]) | **Control** Success Rate (Range[1]) |
| **Overall Success[2]** | 68% (60% to 74%) | 61% (48% to 75%) |
| **Fusion** | 94% (63% to 97%) | 86% (68% to 99%) |
| **NDI Pain/Disability Improvement** | 75% (68% to 81%) | 75% (62% to 87%) |
| **Neurological Status Maintenance or Improvement** | 96% (87% to 100%) | 78% (45% to 92%) |

[1] There is a 95% probability that success rates will fall between the ranges listed.
[2] See Section XI.D. for the definitions of success used in this study.

In Table VIII, neurological success is defined as success in 3 of the 4 subsections (sensory, motor, reflex, and foraminal compression test) as per the protocol. If neurological success were redefined to require successes in 4 of 4 subsections, 13 of 171 AFFINITY™ device patients and 16 of 45 control patients would not be a neurological success. Of the 13 AFFINITY™ patients, there were ten patients with reflex deficits and three with sensory deficits. Eight of these deficits are associated with the operative or adjacent levels.

## 2. Safety Analysis

Safety analyses included all patients regardless of the completeness of their follow-up data or length of follow-up. Table II summarizes all adverse events which occurred in the AFFINITY™ device and control patients. A majority of the adverse event rates and secondary surgery rates were comparable between the groups.

## 3. Effectiveness Analysis—Intent-To-Treat

An "intent-to-treat" analysis of the AFFINITY™ group was also performed. For this analysis, secondary surgery failures, deaths, and missing observations due to other causes resulted in missing observations for the outcome variables and therefore were included in the denominators of the calculated rates, i.e., considered as "failures". By treating these unobserved data as treatment failures, the clinical outcome rates in the intent-to-treat analysis naturally will be lower than the rates reported in the actual observed clinical data. Table IX provides the results for the intent-to-treat analysis.

| Table IX - Intent-to-Treat Analysis for AFFINITY™ Device Deaths, Secondary Surgery Failures, and Missing Observations Are Considered as Failures and Are Included in the Denominator of the Rates | |
|---|---|
| | **24 Month Rates** |
| **Fusion** | 77.7% (157/202) |
| **NDI Pain/Disability Improvement** | 67.3% (136/202) |
| **Neurological Status Maintenance or Improvement** | 83.7% (169/202) |
| **Overall Success** | 60.9% (123/202) |

## XII. CONCLUSIONS DRAWN FROM THE STUDIES

Overall success (i.e., fusion, a successful pain and disability outcome, neurological success as well as the patient not having a secondary surgery classified as a revision, removal or supplemental fixation) was the primary endpoint for the clinical trial and it is the parameter on which the success of the clinical trial is determined. The overall success rate for the AFFINITY™ device group was found to be at least statistically equivalent to the autograft control group rate.

The AFFINITY™ device was found to be at least as safe as the control treatment. A majority of the adverse event rates and secondary surgery rates were comparable between the groups.

The results of the clinical study provide reasonable assurance that the AFFINITY™ Anterior Cervical Cage System is safe and effective for the indicated patient population.

## XIII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Orthopedic and Rehabilitation Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicated information previously reviewed by this panel.

## XIV. CDRH DECISION

FDA issued an approval order on June 13, 2002. The applicant's manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

The PMA for the AFFINITY™ Cage was granted expedited review status on August 31, 2000, because the device potentially represented a clinically meaningful advantage over existing technology.

## XV. APPROVAL SPECIFICATIONS

Directions for Use: See product labeling.

Hazard to Health from Use of the Device: See Indications, Contraindications, Precautions, and Adverse Events in the labeling.

Post Approval Requirements and Restrictions: See Approval Order.

## XVI. REFERENCES


1 "An Experimental Study of the Immediate Load Bearing Capacity of Three Surgical Constructions for Anterior Spine Fusions", White III, A.A., Jupiter, J., Southwick, W.O., Panjabi, M.M., *CORR*, No. 91, pp. 21-28, March-April 1973.

2 "Compressive Strength of Autogenous and Allogenous Bone Grafts for Thoracolumbar and Cervical Spine Fusion", Wittenberg, R.H., Moeller, J., Shea, M., and White III, A.A., *Spine*, Vol. 15, No. 10, pp. 1073-1078. 1990.

3 Clinical Biomechanics of the Spine, 2nd Edition, White III, A.A. and Panjabi, M.M., J.B. Lippincott Company, Philadelphia, 1990.